UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/491,624	01/26/2000	Carlos Picornell Darder	4948-2P/C/RCE	8816

7590 05/29/2008

THOMAS C. PONTANI, ESQ.
COHEN PONTANI LIEBERMAN & PAVANE
551 FIFTH AVENUE
SUITE 1210
NEW YORK, NY 10176

EXAMINER	
LANDAU, SHARMILA GOLLAMUDI	

ART UNIT	PAPER NUMBER
1611	

MAIL DATE	DELIVERY MODE
05/29/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

UNITED STATES PATENT AND TRADEMARK OFFICE

Commissioner for Patents
United States Patent and Trademark Office
P.O. Box 1450
Alexandria, VA 22313-1450
www.uspto.gov

BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Application Number: 09/491,624
Filing Date: January 26, 2000
Appellant(s): DARDER, CARLOS PICORNELL

Vincent Fazzari
Reg. No. 26,879
For Appellant

EXAMINER'S ANSWER

This is in response to the appeal brief filed March 4/2008 appealing from the Office action mailed July 27, 2007.

(1) Real Party in Interest

A statement identifying by name the real party in interest is contained in the brief.

(2) Related Appeals and Interferences

The examiner is not aware of any related appeals, interferences, or judicial proceedings which will directly affect or be directly affected by or have a bearing on the Board's decision in the pending appeal.

(3) Status of Claims

The statement of the status of claims contained in the brief is correct.

(4) Status of Amendments After Final

The appellant's statement of the status of amendments after final rejection contained in the brief is correct.

(5) Summary of Claimed Subject Matter

The summary of claimed subject matter contained in the brief is correct.

(6) Grounds of Rejection to be Reviewed on Appeal

The appellant's statement of the grounds of rejection to be reviewed on appeal is substantially correct. The changes are as follows:

Rejection 4. Claims 47, 48 and 50 under 35 USC §103(a) as unpatentable over DePui '184 in view of Wurster in view of U.S. Patent No. 5,232,706 to Palomo further in view of U.S. Patent No. 5,219,870 to Kim et al.

(7) Claims Appendix

The copy of the appealed claims contained in the Appendix to the brief is correct.

(8) Evidence Relied Upon

6,132,771	DEPUI et al	10-2000
6,365,184	DEPUI et al	4-2002
2,799,241	WURSTER	7-1957
4,017,647	OHNO et al	4-1977
5,219,870	KIM	6-1993
5,232,706	PALOMO	8-1993
96/01624	BERGSTRAND et al	1-1996

(9) Grounds of Rejection

The following ground(s) of rejection are applicable to the appealed claims:

(A) Claims 15-16, 18-25, 30-31, 33-34, 36, 39-46, 49 are rejected under 35 U.S.C. 103(a) as being unpatentable over US Patent 6,365,184 to Depui et al by itself or in view of Wurster (2,799,241).

Depui et al teach an oral pharmaceutical dosage form comprising a proton pump inhibitor and an NSAID (abstract). More specifically, Depui et al teach that the proton pump inhibitor can be selected from **omeprazole, lansoprazole, pantoprazole, pariprazole, and leminoprazole (instant active)**. See column 4 to 6. Additionally, Depui teaches that the core material for their composition is a seed layered with the proton pump inhibitor along with an enteric coating. See column 8, lines 48-50. Depui et al. also disclose that the seeds can be made of different materials, including sugars and mixtures thereof. See column 8, line 58. The reference discloses mixing the proton pump inhibitor with other components prior to layering on the seeds, wherein the components can include binders, surfactants, disintegrating agents, and fillers. See column 9,

lines 1-5. The binder can be selected from HPM, HPMC, HMC, PVP, sugars and starches. See column 9, lines 3-6.

The alkaline substance **(alkaline reacting compound)** can be selected from sodium, potassium, calcium, magnesium and aluminum salts or phosphoric acid, carbonic acid, citric acid or other suitable weak inorganic or organic acids; aluminum hydroxide/sodium bicarbonate co precipitate; substances normally used in antacid preparations such as aluminum, calcium and magnesium hydroxides; magnesium oxide or composite substances, such as Al.sub.2 O.sub.3 0.6MgO.CO.sub.2 0.12H.sub.2 O, (Mg.sub.6 Al.sub.2 (OH).sub.16 CO.sub.3 0.4H.sub.2),MgO.Al.sub.2 O.sub.3 0.2SiO.sub.2.nH.sub.2 O or similar compounds; organic pH-buffering substances such as trihydroxymethylaminomethane, basic amino acids and their salts or other similar, pharmaceutically acceptable pH-buffering substances. See column 9, lines 27-42. The surfactant disclosed is sodium lauryl sulfate. See column 9, lines 10. Lactose monohydrate and mannitol are utilized in the examples.

Depui et al disclose that the seeds have a size between 0. 1 and 2 mm, which equals 100 to 2000 micrometers. See column 8, line 62. Most importantly, Depui et al state that their formulation does not necessarily include a spacing layer between the coated seed and an enteric coating. Depui et al disclose the middle, separating layer is optional, and the enteric coating can be applied directly to the coated core. Depui et al. disclose the optionally applied separating layer(s) is not essential for the invention. See column 9, lines 46-50 and column 10, lines 41-43. The enteric coating layer is selected from I-IPMCP, methacrylic acid polymers, HPMC acetate succinate, and shellac. See column 10, lines 46-53. Further, the enteric coating layer includes a plasticizer: PEG or cetyl alcohol, anti-tacking agents, and pigments. See column 10, lines 58-60

and column 11, lines 1-10. Depui teaches using suitable equipment such as a coating pan, coating granulator, or a fluidized bed apparatus to apply the coats.

Examples 2 utilizes a fluid bed apparatus to coat the inert seeds with the active. The inert seed is coated with a water suspension containing hydroxypropylmethylcellulose (binder); polysorbate 80 (surface active agent); and **omperazole (instant active) magnesium (alkaline reacting compound)**. Note this forms a “charged nucleus" since Appellant discloses on page 15 of the instant specification that spraying a inert nuclei excipient such as a binder, surface active agent, or filler or alkaline reaction compound with the active form a “charged nuclei.” An inert nuclei is disclosed as a neutral granule on page 10, line 8 of the instant specification.

Example 4 utilizes a fluid bed apparatus to coat the inert seeds with the active. The inert seed is coated with a water suspension containing hydroxypropylmethylcellulose (binder); sodium lauryl sulfate (surface active agent); and lansoprazole. Note this forms a “charged nucleus". Then a **Wurster-equipped fluidized apparatus** is used to sub-coat the separating layer, followed by coating an enteric coating using the same equipment. See example 4. Further, arginine is utilized in example 4.

Although example 4 teaches the use of a fluidized bed apparatus in all three steps and Depui teaches the specific use of a Wurster-equipped fluidized apparatus in the second and third step, it is unclear if the same apparatus, i.e. a Wurster-equipped fluidized apparatus, is used in the first step. Depui teaches using a fluidized bed apparatus in the first step without specifying the type.

Wurster teaches the Wurster-type fluidized apparatus provides for a uniformed coating preventing the coating material from sticking to the inner surface of the chamber. See column 1, lines 22-35.

However, it would have been obvious to one of ordinary skill in the art at the time the invention was made to look to the guidance provided by Depui and utilize a Wurster-equipped fluidized apparatus in all three steps since Depui teaches layering may be done by three different types of processes: 1) a coating pan; 2) coating granulator; 3) or a fluidized bed apparatus. Thus, although Depui does not specify that the fluidized bed apparatus in the first step is Wurster-equipped, it is the examiner's position that since all three steps are utilizing a similar process of spray coating using a similar apparatus, i.e. a fluidized bed apparatus, the process is prima facie obvious. Further, it would have been obvious to also use the Wurster-type fluidized bed apparatus in the first step with a *reasonable* expectation of similar results and success since Depui teaches the use of a fluidized bed apparatus without specificity in the first step and the Wurster-type used in the second and third step is also a fluidized bed apparatus that functions to coat the pellet. Thus, regardless of the fluidized apparatus being a Wurster-type, the same end result is yielded, wherein the core is coated.

Alternatively, it would have been obvious to look at Wurster and utilize the instant apparatus in the first step. One would have been motivated to do so since Wurster teaches that the Wurster-type provides a uniform coating. Thus, a skilled artisan would have been motivated to use the same apparatus in the first step to provide a uniform coating so that all three coatings would uniformly be applied. Further, the Wurster patent demonstrates that the Wurster-Type apparatus is not a new type of apparatus and as been known in the art since the 1940s. Therefore,

it is reasonable for a skilled artisan to utilize a conventional machine routinely utilized in the pharmaceutical coating art.

(B) Claims 15-16, 18-25, 30-31, 33-34, 36, 39-46, 49 are rejected under 35 U.S.C. 103(a) as being unpatentable over US Patent 6,132,771 to Depui et al in view of Ohno et al (4,017,647) or Wurster (2,799,241) respectively.

Depui et al teach an oral pharmaceutical dosage form comprising a proton pump inhibitor (abstract). More specifically, Depui et al teach that the proton pump inhibitor can be selected from **omeprazole, lansoprazole, pantoprazole, pariprazole, and leminoprazole (instant active)**. See column 4 to 6. Additionally, Depui teaches that the core material for their composition is a seed layered with the proton pump inhibitor along with an enteric coating. See column 8, lines 48-50. Depui et al. also teach that the seeds can be made of different materials, including sugars and mixtures thereof. See column 8, line 58. The reference discloses mixing the proton pump inhibitor with other components prior to layering on the seeds, wherein the components can include binders, surfactants, disintegrating agents, and fillers. See column 9, lines 1-5. The binder can be selected from HPM, HPMC, HMC, PVP, sugars and starches. See column 9, lines 3-6.

The alkaline substance **(alkaline reacting compound)** can be selected from sodium, potassium, calcium, magnesium and aluminum salts or phosphoric acid, carbonic acid, citric acid or other suitable weak inorganic or organic acids; aluminum hydroxide/sodium bicarbonate co precipitate; substances normally used in antacid preparations such as aluminum, calcium and magnesium hydroxides; magnesium oxide or composite substances, such as Al.sub.2 O.sub.3 0.6MgO.CO.sub.2 0.12H.sub.2 O, (Mg.sub.6 Al.sub.2 (OH).sub.16 CO.sub.3 0.4H.sub.2),

MgO.Al.sub.2 O.sub.3 0.2SiO.sub.2.nH.sub.2 O or similar compounds; organic pH-buffering substances such as trihydroxymethylaminomethane, basic amino acids and their salts or other similar, pharmaceutically acceptable pH-buffering substances. See column 9, lines 27-42. The surfactant disclosed is sodium lauryl sulfate. See column 9, lines 10. Lactose monohydrate and mannitol are utilized in the examples. The instant plasticizers are taught.

Depui et al teach that the seeds have a size between 0. 1 and 2 mm, which equals 100 to 2000 micrometers. See column 8, line 62. Most importantly, Depui et al state that their formulation does not necessarily include a spacing layer between the coated seed and an enteric coating. Depui et al disclose a middle separating layer is **optional**, and the enteric coating can be applied directly to the coated core. See column 9, lines 46-50 and column 10, lines 41-43. The enteric coating layer is selected from I-IPMCP, methacrylic acid polymers, HPMC acetate succinate, and shellac. See column 10, lines 46-53. Further, the enteric coating layer includes a plasticizer: PEG or cetyl alcohol, anti-tacking agents, and pigments. See column 10, lines 58-60 and column 11, lines 1-10. Example 1 teaches suspension layering the inert seed with a water suspension comprising **magnesium (alkaline reacting compound) omperazole** (instant active), hydroxypropylmethylcelllulose (binder). Note this forms a “charged nucleus" since Appellant discloses on page 15 of the instant specification that spraying a inert nuclei excipient such as a binder, surface active agent, or filler or alkaline reaction compound with the active form a “charged nuclei.” An inert nuclei is disclosed as a neutral granule on page 10, line 8 of the instant specification.

Depui et al do not specify the type of fluidized bed apparatus utilized.

Ohno et al teach a method for providing an enteric coating on solid dosage forms. The enteric coating solution contains those taught in Depui et al, i.e. film-forming polymers (HPMC), plasticizers, pigments, etc. on column 2. Ohno et al teach the use of a conventional coating machine such as pan coaters, drum-type coaters, or Wurster-type fluidizing coaters, and Glatt fluidizing coater since there is no principle difference between coating solid dosage forms and all conventional coaters work under the same principle of utilizing a coating solution. See column 3, lines 24-40.

Wurster teaches the Wurster-type fluidized apparatus provides for a uniformed coating, which prevents the coating material from sticking to the inner surface of the chamber. See column 1, lines 22-35.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to combine the teaching of Depui et al and Ohno et al and utilize the fluidized apparatus of choice such as instant Wurster-type. One would have been motivated to do so since Ohno teaches that the Wurster-type apparatus among other fluid bed coaters are known and conventionally utilized in the art for coating purposes and all the coating machines work under the same principle. Therefore, it is prima facie obvious to utilize the instant Wurster-Type in Depui's process with a reasonable expectation of success since not only does Depui teach the use of a fluid bed apparatus but Ohno teaches the equivalency of all coating machines.

Further, it would have been obvious to look at Wurster and utilize the instant apparatus. One would have been motivated to do so since Wurster teaches that the Wurster-type provides a uniform coating. Further, the Wurster patent demonstrates that the Wurster-Type apparatus is not a new type of apparatus and as been known in the art since the 1940s. Therefore, it is reasonable

for a skilled artisan to utilize a conventional machine routinely utilized in the pharmaceutical coating art.

(C) Claims 15-16, 18-25, 30-31, 33-34, 36, 39-46, 49 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO 96/01624 in view of Ohno et al (4,017,647) or Wurster (2,799,241).

WO 96/01624 teaches instant proton pump inhibitor (Formula I) in an oral dosage form comprising an inert core layered with the active agent, an optional separating layer, and an enteric layer. See examples and page 17, lines 24-30. The core may be prepared by spray drying. See page 12, lines 24-25. The inert seed is made of sugar, nonpareils, etc alone or in mixtures and is 0.1-2mm. The inert seed is spray coated, using a layering equipment, with the instant active agent which is combined with other components such as binders, surfactants, instant fillers, surfactants, etc. see page 11, lines 5-26.

WO 96/01624 teaches the instant proton pump inhibitor may be used in the neutral form or mixed with an alkaline salt **(alkaline reacting compound)** such as sodium, potassium, calcium, and Al2O3, 6MgOCO2, MgOAl2 O 3, and basic amino acids. See page 5, lines 1-5 and page 12, lines 10-20. The instant enteric coating polymers are taught on page 13, lines 14-25 and the instant plasticizers are taught on page 15, lines 1-2. WO teaches the use of a fluid bed apparatus. Note examples, especially 1, wherein steps a) to c) are spray coated using a fluid bed apparatus. A water suspension comprising **lansoprazole (instant active)** and binder are coated onto an inert seed. Example 11 teaches the core material without a separating layer. Note this forms a “charged nucleus" since Appellant discloses on page 15 of the instant specification that spraying a inert nuclei excipient such as a binder, surface active agent, or filler or alkaline

reaction compound with the active form a "charged nuclei." An inert nuclei is disclosed as a neutral granule on page 10, line 8 of the instant specification. Reference example III uses magnesium (alkaline reacting compound) omeprazole (Formula I).

WO does not specify the type of fluidized bed apparatus utilized.

Ohno et al teach a method for providing an enteric coating on solid dosage forms. The enteric coating solution contains those taught in Depui et al, i.e. film-forming polymers (HPMC), plasticizers, pigments, etc. on column 2. Ohno et al teach the use of a conventional coating machine such as pan coaters, drum-type coaters, or Wurster-type fluidizing coaters, and Glatt fluidizing coater since there is no principle difference between coating solid dosage forms and all conventional coaters work under the same principle of utilizing a coating solution. See column 3, lines 24-40.

Wurster teaches the Wurster-type fluidized apparatus provides for a uniformed coating which prevents the coating material from sticking to the inner surface of the chamber. See column 1, lines 22-35.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to combine the teaching of WO '624 and Ohno et al and utilize the fluidized apparatus of choice such as instant Wurster-type. One would have been motivated to do so since Ohno teaches that the Wurster-type apparatus among other fluid bed coaters are known and conventionally utilized in the art for coating purposes and all the coating machines work under the same principle. Therefore, it is prima facie obvious to utilize the instant Wurster-Type in WO's process with a reasonable expectation of success since not only does WO teach the use of a fluid bed apparatus but Ohno teaches the equivalency of all coating machines.

Further, it would have been obvious to look at Wurster and utilize the instant apparatus. One would have been motivated to do so since Wurster teaches that the Wurster-type provides a uniform coating. Further, the Wurster patent demonstrates that the Wurster-Type apparatus is not a new type of apparatus and as been known in the art since the 1940s. Therefore, it is reasonable for a skilled artisan to utilize a conventional machine routinely utilized in the pharmaceutical coating art.

(D) Claims 47-48 and 50 are rejected under 35 U.S.C. 103(a) as being unpatentable over US Patent to Depui et al (6,365,184) in view of Wurster (2,799,241) in view of Palomo (5,232,706) in further view of Kim et al (5,219,870).

US '184 has been delineated above. The references teach mixing the proton pump inhibitor with an alkaline substance selected from sodium, potassium, calcium, magnesium and aluminum salts or phosphoric acid, carbonic acid, citric acid or other suitable weak inorganic or organic acids; aluminum hydroxide/sodium bicarbonate co precipitate; substances normally used in antacid preparations such as aluminum, calcium and magnesium hydroxides; magnesium oxide or composite substances, such as Al.sub.2 O.sub.3 0.6MgO.CO.sub.2 0.12H.sub.2 O, (Mg.sub.6 Al.sub.2 (OH).sub.16 CO.sub.3 0.4H.sub.2),MgO.Al.sub.2 O.sub.3 0.2SiO.sub.2.nH.sub.2 O or similar compounds; organic pH-buffering substances such as trihydroxymethylaminomethane, basic amino acids and their salts or other similar, pharmaceutically acceptable pH-buffering substances.

US '184 do not teach the instant amino acid in the core material.

Palomo teaches an oral pharmaceutical preparation of omeprazole wherein omeprazole may be mixed with a basic compound such as sodium, potassium, magnesium, calcium,

aluminum or dihydroxyaluminium salts of amino acids, such as glycocoll (pKa.sub.2 =9.6), glutamic acid (pKa.sub.3 =9.67) or lysine (pKa.sub.2 =8.9, pKa.sub.3 =10.28), or a pyridine carboxylic acid, such as nicotinic acid, or they are organic bases, such as guanidine (pK=12.5) or a salt of said bases with an weak organic or inorganic acid, for example guanidine carbonate, guanidine sodium carbonate, guanidine phosphate or guanidine disodium phosphate, arginine, histidine, or lysine to achieve stabilization of omeprazole in the nucleus and to isolate it more effectively from the external acidity. See column 2, lines 25-45.

Kim teaches the use of amino acids in general and specifically arginine, histidine, or lysine provides stability to omeprazole and prevents it from changing colors during storage. See abstract, column 3, lines 1-10, column 5-6, and example 2.

It would have been obvious to one of ordinary skill in the art at the time the invention was made combine the teachings of the above references and specifically utilize the claimed amino acids. One would have been motivated to do so with a reasonable expectation of success since Depui teaches the general use of an alkaline substance such as amino acids with the core material and the proton pump inhibitor (omeprazole) and Palomo teaches the instant amino acids are suitable for use with omeprazole to stabilize it. Furthermore, a skilled artisan would have been motivated to utilize the instant amino acids as the alkaline substance since Kim teaches amino acids, specifically arginine, histidine, or lysine provides stability to omeprazole and prevents it from changing colors during storage.

(E) Claims 47-48 and 50 are rejected under 35 U.S.C. 103(a) as being unpatentable over US Patent to Depui et al (6,132,771) or WO 96/01624 respectively, in view of Ohno et

al (4,017,647) or Wurster (2,799,241) respectively, in view of Palomo (5,232,706) in further view of Kim et al (5,219,870).

US '771 and WO '624 have been delineated above. The references teach mixing the proton pump inhibitor with an alkaline substance selected from sodium, potassium, calcium, magnesium and aluminum salts or phosphoric acid, carbonic acid, citric acid or other suitable weak inorganic or organic acids; aluminum hydroxide/sodium bicarbonate co precipitate; substances normally used in antacid preparations such as aluminum, calcium and magnesium hydroxides; magnesium oxide or composite substances, such as Al.sub.2 O.sub.3 0.6MgO.CO.sub.2 0.12H.sub.2 O, (Mg.sub.6 Al.sub.2 (OH).sub.16 CO.sub.3 0.4H.sub.2),MgO.Al.sub.2 O.sub.3 0.2SiO.sub.2.nH.sub.2 O or similar compounds; organic pH-buffering substances such as trihydroxymethylaminomethane, basic amino acids and their salts or other similar, pharmaceutically acceptable pH-buffering substances.

US '771 and WO '624 do not teach the instant amino acid in the core material.

Palomo teaches an oral pharmaceutical preparation of omeprazole wherein omeprazole may be mixed with a basic compound such as sodium, potassium, magnesium, calcium, aluminum or dihydroxyaluminium salts of amino acids, such as glycocoll (pKa.sub.2 =9.6), glutamic acid (pKa.sub.3 =9.67) or lysine (pKa.sub.2 =8.9, pKa.sub.3 =10.28), or a pyridine carboxylic acid, such as nicotinic acid, or they are organic bases, such as guanidine (pK=12.5) or a salt of said bases with an weak organic or inorganic acid, for example guanidine carbonate, guanidine sodium carbonate, guanidine phosphate or guanidine disodium phosphate, arginine, histidine, or lysine to achieve stabilization of omeprazole in the nucleus and to isolate it more effectively from the external acidity. See column 2, lines 25-45.

Kim teaches the use of amino acids in general and specifically arginine, histidine, or lysine provides stability to omeprazole and prevents it from changing colors during storage. See abstract, column 3, lines 1-10, column 5-6, and example 2.

It would have been obvious to one of ordinary skill in the art at the time the invention was made combine the teachings of the above references and specifically utilize the claimed amino acids. One would have been motivated to do so with a reasonable expectation of success since Depui teaches the general use of an alkaline substance such as amino acids with the core material and the proton pump inhibitor (omeprazole) and Palomo teaches the instant amino acids are suitable for use with omeprazole to stabilize it. Furthermore, a skilled artisan would have been motivated to utilize the instant amino acids as the alkaline substance since Kim teaches amino acids, specifically arginine, histidine, or lysine provides stability to omeprazole and prevents it from changing colors during storage.

(10) Response to Argument

(A) Claims 15-16, 18-25, 30-31, 33-34, 36, 39-46, 49 are rejected under 35 U.S.C. 103(a) as being unpatentable over US Patent 6,365,184 to Depui et al by itself or in view of Wurster (2,799,241).

Appellant states that the instant anti-ulcer compounds are known to be acid labile and degrade rapidly in an acidic environment. Appellant explains that when such compounds are exposed to the gastric environment, they can rapidly degrade within the stomach. Therefore, Appellant explains that enteric coatings are used to protect a dosage form from stomach acid. However, Appellant states that the acids in the coating cause premature degradation of the compounds of Formula I. Thus, Appellant explains that the prior art uses techniques used to

protect the active is to include an alkaline substance. However, the interaction of the alkaline substance and the enteric coating causes the break down of the enteric coating and exposing the active to the stomach acid. Therefore, Appellant argues that Depui '184 requires the anti-ulcer compound and the alkaline material require a separating layer between the enteric coating and the anti-ulcer compound. Appellant argues that all examples comprise a separating layer between the active layer and enteric coating and the disclosure does not provide a single example or suggestion of how to produce a stable and useful composition.

The examiner respectfully points out the independent process claims 34 and 36 recite **comprising** claim language. MPEP 2111.03 defines the transitional phrase "comprising" as "inclusive or open-ended and does not exclude additional, unrecited elements or method step" Further, MPEP 211.03 clearly states, "The transition 'comprising' in a method claim indicates that the claim is open-ended and allows for a additional steps." The instant process claims do not recite closed claim language and therefore the process claims are not exclusionary, i.e. **the instant claims do not exclude Depui's separating layer or other active ingredients.** Thus, Appellant's arguments pertaining to Depui's use of a separating layer have not been "ignored" as asserted by Appellant. Rather, the examiner' position is that Appellant has not distinguished the instant process claims from the prior art or Appellant has not limited the instant process claims to this purportedly critical and defining aspect (the exclusion of a separating layer).

Appellant argues that the instant claim language clearly limits the scope of the claim to layering the enteric coating directly on the charged nucleus.

First, it is noted that the claims do not recite "directly thereon". Independent claim 34 is directed to:

a) coating an inert nucleus to form a substantially non-porous layer thereon by spraying on the nucleus an aqueous or hydroalcoholic suspension-solution, which comprises: (i) a compound of Formula I, II, or III; (ii) an alkaline reacting compound, and (iii) at least one pharmaceutically acceptable excipient selected from the group consisting of a binder, a surface-active agent, a filling material and a disintegrating-swelling excipient;

b) drying the active layer formed during said spraying to form a charged nucleus; and

c) coating the charged nucleus by spraying a solution which contains an enteric coating polymer with at least one pharmaceutically acceptable excipient to form a gastro-resistant external coating layer on said charged nucleus wherein the steps a) to c) are performed in a Wurster-type fluidized bed coater.

Independent claim 36 is directed to:

a) coating an inert nucleus in a fluidized bed coater to form a substantially non-porous layer thereon by spraying on the nucleus an aqueous or hydroalcoholic suspension-solution, which comprises: (i) an active ingredient of Formula I, II, or III; (ii) an alkaline reacting compound, and (iii) at least one pharmaceutically acceptable excipient selected from the group consisting of: a binder, a surface-active agent, a filling material and a disintegrating-swelling excipient;

b) drying the active layer formed during said spraying to form a charged nucleus in said fluid bed coater; and

c) coating the charged nucleus in the fluid bed coater by spraying on said charged nucleus a solution which contains an enteric coating polymer with at least one pharmaceutically

acceptable excipient to form a gastro-resistant external coating layer thereon, wherein the fluidized bed coater is a Wurster-type fluidized bed coater.

As it can be seen, the claims are not limited to coating the enteric coating ***directly*** to the charged nucleus. Thus, the claim language does not exclude the separating layer. The claims merely state that the "charged nuclei" is sprayed with an enteric coating.

Second, the claims are given their broadest reasonable interpretation. As discussed above the instant claim language "comprising" is not exclusionary. Neither the instant process claims nor Appellant's specification define the "charged nuclei". Thus, "said charged nucleus" itself may include other layers. For instance, the inert nucleus, the drug layer, and the separating layer may be interpreted to form "the charged nucleus". Therefore, claim 34, which recites "gastro-resistant external coating layer on said charged nucleus" and claim 36, which recites "a gastro-resistant external coating layer thereon", does not exclude a separating layer since this separating layer is interpreted to form the charged nuclei.

Appellant argues that the examiner is "engaging in claim construction" and the examiner is only permitted to interpret the claim as broadly and as reasonably supported by the specification. Appellant argues that the specification does not utilize a second active e agent. Appellant argues that it is clear that "comprising" is being used by the PTO to alter, or unreasonably interpret, the limitations expressly stated in the claims. Appellant argues that the record does not contain any case authority or any section of the MPEP which permits the PTO to alter a limitation, or interpret it in a manner inconsistent with the specification or the claim language, because of the use of the transitional phrase "comprising". Appellant argues claims 34 and 36 as pending indicate that the only active is an anti-ulcer compound.

As discussed above, the Patent Office has not construed the term "comprising" in an inconsistent manner or in a manner contrary to the MPEP. The examiner respectfully directs Appellant's attention to MPEP 2111.03, which clearly defines how "comprising" should be interpreted.

> "The transitional term "comprising", which is synonymous with "including," "containing," or "characterized by," **is inclusive or open-ended and does not exclude additional, unrecited elements or method steps.** See, e.g., >*Mars Inc. v. H.J. Heinz Co.*, 377 F.3d 1369, 1376, 71 USPQ2d 1837, 1843 (Fed. Cir. 2004) ("like the term 'comprising,' the terms 'containing' and 'mixture' are open-ended.").< *Invitrogen Corp. v. Biocrest Mfg., L.P.*, 327 F.3d 1364, 1368, 66 USPQ2d 1631, 1634 (Fed. Cir. 2003) (**"The transition 'comprising' in a method claim indicates that the claim is open-ended and allows for additional steps."**); *Genentech, Inc. v. Chiron Corp.*, 112 F.3d 495, 501, 42 USPQ2d 1608, 1613 (Fed. Cir. 1997) ("Comprising" is a term of art used in claim language which means that the named elements are essential, but other elements may be added and still form a construct within the scope of the claim.);

Thus, the examiner's position is supported by the MPEP. However, the MPEP does not support Appellant's assertion that Appellant's disclosure should be relied upon to interpret the claim language "comprising".

Assuming arguendo that the claim excludes a separating layer, the examiner point out that Depui's separating layer is **optional**. The Webster Dictionary defines *optional* as: involving an option: not compulsory. Further, option is defined as: 1) something that may be chosen 2) an item that is offered in addition to or in place of the standard.

Therefore, the word "optional" itself clearly denotes that if one were to exclude the *optional* separating layer, it would not be detrimental to the dosage form.

Appellant argues that if the separating layer is excluded in Depui's dosage form, it would not be stable. Thus, Appellant argues that Depui is not enabled.

The examiner respectfully points out that if the separating layer was absolutely critical to Depui's invention, then Depui would not insert the word "optional".

Appellant argues that the dictionary definition is not favored.

The examiner directs Appellant's attention to MPEP 2111.01, which clearly states that the claims must be given plain meaning unless clearly defined by the specification. Further, "plain meaning" refers to the ordinary and customary meaning given to the term by those skilled in the art. First, it is noted that the instant specification does not define the term "optional'. Second, the examiner respectfully points out that word "optional" is not a term that has a special meaning to those in the art. The examiner merely uses the dictionary definition to denote to Appellant that "optional" implies that it is not necessary. This is further substantiated by Depui disclosure on column 9, lines 46-50 and column 10, lines 41-43, **"the optionally applied separating layer(s) is not essential for the invention."** Every issued patent is presumed to be valid and Appellant has not provided any *persuasive* evidence to the contrary.

Appellant argues that Depui et al does not make a positive statement that a separating layer is not necessary and the examiner merely makes an inference from the use of the word "optional". Again the examiner directs Appellant's attention to column 9, lines 46-50 and column 10, lines 41-43. Depui et al disclose the middle separating layer is **optional** and the enteric coating can be applied directly to the coated core. Depui et al disclose "the optionally applied separating layer(s) is not essential for the invention." This is clearly a "positive statement" that the separating layer is not necessary and it is not an inference made by the examiner.

Appellant argues that Depui et al do not exemplify a dosage form without the optional separating layer.

It is respectfully pointed out that "Disclosed examples and preferred embodiments do not constitute a teaching away form a broader disclosure or nonpreferred embodiment. In re Susi 440 F.2d 442, 169 USPQ 423 (CCPA 1971). Moreover, as discussed above, Depui teaches two options, a dosage form with or without a separating layer. Thus, a skilled artisan can readily envisage the alternative form, i.e. the dosage form without a separating layer.

Appellant argues that the examiner has repeatedly ignored the Declarations by stating they are not persuasive. Appellant argues that a Declaration can be used to demonstrate that the prior art is not enabling. Further, Appellant argues that the examiner has made the rejection under obviousness and thus the declaration must be addressed.

Appellant argues that the Molina affidavit demonstrates that Depui is not enabled. Appellant argues that the Johansson's declaration demonstrates that Depui is not enabling. Appellant argues that the instant example 1 is more stable than Depui's example 5.

First, it is respectfully submitted that Appellant's Declarations and Appellant's arguments in reference to the Declaration are based on the erroneous assertion that the claims exclude a separating layer. It is the examiner's position that the instant claim language does not exclude Depui's separating layer. However, assuming arguendo the claims exclude this layer, the examiner notes the following:

The examiner notes that in the Molina Declaration, Appellant attempts to overcome Depui by showing EP 0642797 does not make a stable granule. It is pointed out that if Appellant contends that the prior art is not enabling, and in instant case, Appellant contends Depui is not

enabling, then the declaration must show that Depui is not enabled. Appellant's demonstration that EP '797 does not make a stable granule does not extend to Depui. Depui is a different invention with no relation to EP '797. Further, **EP '797 teaches a different formulation than Depui.** For instance, EP '797 contains excipients used to coat the inert seed that are not utilized in Depui's examples. These excipients may contribute to the lack of stability. For instance, starch is a known disintegrant. The formulations of Depui and EP '797 are not the same. Appellant has not addressed this.

Moreover, it is the Appellant's position that it is not Appellant's burden but the examiner's burden to demonstrate how these excipients cause instability. The examiner respectfully points out that the standard for demonstrating that an issued US patent is not enabling is not only high, but it is Appellant's burden and not the examiner's. The examiner can only determine enablement of the prior art, or conversely, lack thereof, by the evidence given by Appellant. The examiner notes the differences in the formulations which cause the evidence provided by Appellant to be not persuasive since it does not conclusively demonstrate that Depui is not enabled. The examiner has satisfied the criteria of analyzing the evidence to determine if the prior art is enabled for certain embodiments; however Appellant has not satisfied Appellant's burden of demonstrating why these additional excipients disclosed in EP '797 and the difference in the dosage form do not have a bearing on the issue of enablement. Appellant's refusal and failure to show that *Depui's* dosage form is perplexing since it is Appellant that is attempting to demonstrate that Depui is not enabled for certain embodiments. Thus, it is the examiner's position that Appellant must demonstrate that Depui's dosage form, not other prior art dosage forms, are not stable.

Regarding the Johansson's Declaration, the Declaration states, "The results obtained in working Example 5 of US 6.132.771 where not a surprise for me, because the prior art, for instance EP0247983 (US 4,786,505) and EP244380 (US 4,853,230) cited in the patent application taught that an inert separating layer should be place between the core material and the outer enteric coating layer to avoid the contact between the anti-ulcer benzimidazole compound (omeprazole, lansoprazole, pantoprazole. etc.) and the acidic component (methacrylic copolymer) of the enteric layer. It is also mentioned that benzimidazole compounds are not stable in acidic medium, and in contact with acidic compounds they suffer degradation and develop a strong color."

First, it is pointed out that the instant rejection is made over US 6,365,184 and not US 6,132,771. This is a critical difference since US 6,365,184 to Depui et al uses a fluid bed apparatus, specifically a Wurster fluidized apparatus, to make the composition. Appellant has repeatedly argued that Appellant's apparatus (Wurster fluidized apparatus) provides the "unexpected stability". Thus, Appellant must show that US '184 is not enabling since clearly US '184 utilizes Appellant's apparatus. A purported showing that US '771 is not enabled does not extend to Depui '184.

Secondly, the examiner notes the following: The instant invention *as claimed* is directed to the same dosage as disclosed by Depui et al. For instance, Appellant argues that the instant invention does not require Depui's optional separating layer and still is stable. Assuming arguendo that the claims do exclude the separating layer, the examiner notes that the instantly claimed invention requires the core material that comprises the anti-ulcer benzimidazole compound (omeprazole, lansoprazole, pantoprazole. etc.), an alkaline reaction compound, and an

enteric coating polymer wherein the instant examples in the specification utilize an acidic polymer. The prior art also discloses this, except the prior art exemplifies an optional separating layer. It is unclear how the instant formulation is stable versus the prior art's formulation if the only difference is the separating layer, which Appellant argues provides stability to Depui's dosage form. The same dosage form is being claimed; thus the same interaction must take place. The examiner points out that the distinguishable feature must be claimed since Appellant's arguments are on the basis that the prior art is not enabled for a stable formula and the instant invention is. If Appellant removes the stabilizing separating layer of the prior art, what makes the instant invention stabilizing without it? It is further noted that the instant specification does not utilize an alkaline material in combination with the anti-ulcer drug. As argued by Appellant in the background section page 5 of the Appeal Brief, Appellant argues that the alkaline material used to protect the active in the active layer, interacts with the enteric coating to cause degradation. Thus, Appellant stated the prior art requires a separating layer. Therefore, it is noted that Appellant discloses and claims the same dosage form as the prior art and yet argues that the prior art is not enabling. Thus, like Depui, Appellant has not exemplified a dosage form comprising an active layer comprising the alkaline material and anti-ulcer compound without a separating layer.

Appellant attributes the stability to the non-porous layer and argues that Depui does not teach this.

Although Depui does not explicitly state that the layer is substantially non-porous layer, Depui's layer is the same as Appellant's. Thus, Depui's active layer must be substantially non-porous. Appellant argues that Depui's active layer is porous but does not specify what exactly

makes it porous. First, it is noted that "substantially" is a broad term and is not defined by the specification. Depui's active layer has the same components as the instant claims and the examples disclosed in Appellant's specification; thus it is the examiner's position that it is non-porous. The claims are directed to "a *substantially* non-porous active layer made from aqueous or hydroalcoholic solution suspension which comprises an anti-ulcer compound, an alkaline reacting compound, and at least one pharmaceutically acceptable excipient selected from the groups which includes a binder, a surface active agent, a filling material, and a disintegrating swelling excipient". Depui discloses the seeds (inert nucleus) are layered with a water suspension comprising the instant anti-ulcer compound, with the alkaline material, a binder, and surface active agent (surfactant). It is respectfully submitted that when the structure of the prior art is substantially identical to the instant claims; the properties must be the same. The examiner has made a reasonable rationale as to why the active layer is substantially non-porous. However, Appellant has not provided any evidence showing that Depui's layer is not substantially non-porous. Appellant has not even provided any persuasive argument, other than the "prior art does not teach a substantially non-porous layer", why Depui's active layer is not substantially non-porous layer.

Appellant attributes the instant invention's stability to the process of making the composition. Appellant has argued that the process of making the instant invention, i.e. utilizing a Wurster fluidized bed coater, lends to the stability (Response of 10/31/05, 12/3/04 and affidavit of 11/22/02).

However, it is noted that Depui also uses a fluid bed apparatus and specifically a Wurster-fluidized apparatus in example 4. Although, it is unclear if the same apparatus is used in

all three steps, it is the examiner's position that the process will yield a similar result since the same type of machine is used. It is noted on page 16 of the instant specification. Appellant discloses that a Wurster-type fluid bed apparatus "or a similar equipment" may be used. Appellant has not compared a process using specifically Wurster-type fluidized apparatus compared to another process using a fluidized bed apparatus. Moreover, Appellant has not provided any evidence that using a Wurster-type fluidized bed apparatus in all three steps compared to using a unspecified fluidized bed apparatus in the first step, followed by using the instant Wurster-type fluidized apparatus provides any unexpected product. For instance, the Rule 132 declaration compares the stability of Depui's formulation US '771 with or without the separating layer to show that Depui '184 is purportedly non-enabling. However, the Declaration does not provide any unexpected results pertaining to the apparatus itself. Further, it is unclear from this Declaration and results if Appellant's stability is due to the Wurster bed coater. The examiner has suggested that Appellant provide evidence wherein two formulas with the same components are made by different apparatuses since this is the purported difference. However, Appellant has not done so.

The Johansson and Molina-Millian Declarations state that the prior art's tablets are discolored compared to the instant invention and this discoloration shows a degradation of the active which is unacceptable.

The examiner respectfully submits that the standard for demonstrating that a reference is not enabling, is high. To demonstrate that a reference is not enabling, the Appellant must demonstrate that a pellet cannot be made. Clearly, a pellet was made, regardless of the color. Regarding the showings of unexpectedness to overcome the 103 rejection, it is pointed out that

the discoloration only appeared **after an hour**. The claims do not recite stability parameters, i.e. how long the instant pellets are stable for. Clearly, as evidenced by the declaration, Depui's pellets are stable for at least one hour.

Appellant argues that recited benefits should not be recited in the claims.

Appellant has misinterpreted the examiner. The examiner is merely pointing out that Appellant's assertion that Depui is not enabled since it is not stable is erroneous since the pellet is clearly stable for an hour. Therefore, Depui meets the claimed limitations of dependent claims 39-40 since the claims merely recite the "preparation is stable" without any specific parameters.

Moreover, Appellant's Declaration is solely based on color to show degradation of the active. However, discoloration does not necessarily imply that the active has degraded. The discoloration may be due to the interaction of other components. Appellant has not provided any data showing a chemical analysis of the active and its purported degradation. The mere assertion that the discoloration means that the active has degraded is not enough to show that the prior art is not stable and thus not enabled.

Appellant argues that the Lovgren Patent (US 4786505) indicates that discoloration means degradation. Appellant states that the examiner hypothesizes that the source of degradation is from another source other than degradation. However, Appellant argues that the examiner has not provided any evidence to support such an assertion.

Again, the examiner respectfully points out that it is Appellant's burden and not the examiner's burden to show that the prior art is not enabled. The examiner can only make an analysis based on the evidence provided by Appellant's. The examiner has made such an analysis and has found the evidence insufficient to conclusively demonstrate that Depui is not

enabled. A patent is presumed to be valid. Thus, the examiner is not required to prove that the prior art relied upon is enabled. If Appellant is attempting to demonstrate that Depui is not enabled for certain embodiments, then it is Appellant's burden to do so. Appellant has not shown conclusively that discoloration necessarily means that the active has degraded. The examiner notes that Lovgren in fact teaches that although some pellets have a slight discoloration, the pellets were stable. Note the examples.

Furthermore, it is noted that the claims are not commensurate in scope. Appellant relies on example 1 of the instant specification to demonstrate that the prior art is not enabled and that the instant invention is unexpectedly stable. Example 1 of the instant specification discloses a charged nucleus and the enteric coating with specific materials whereas the instant claims are broadly directed at least one excipient. As discussed above, Appellant claims the same dosage form and states the difference between the prior art and the instant invention is the use of a separating layer. Further, Appellant argues this separating layer in the prior art functions to provide stability. Thus, the question is, how does obtain a stable pellet by removing the stabilizing stable layer? It is noted that in inventive example 1, the charged nucleus and the enteric coat comprises the components of the prior art's separating layer. For instance, the Depui's separating layer (example 4) comprises HPMC, PEG 6000, and talc whereas although the instant invention excludes the separating layer, the charged nucleus composition comprises HPMC and the enteric coating composition comprises talc and PEG 6000. Thus, if Appellant's stability is due to adding the very components that comprises the prior art's separating layer, to the charged nucleus and enteric coating respectively (thus eliminating the need for the prior art's separating layer), then Appellant must claim this. Further, specific excipients are utilized in

specific concentrations and it is unclear if the excipient and its concentrations contribute to the stability of the instant invention. Lastly, the examiner notes that Appellant's independent claims are drawn to several different classes of compounds and Appellant emphasizes the stability of the compounds. Appellant's Rule 132 is directed to a single species lanzoprazole in a specific formula. However, a single species cannot extend patentability to the entire genus and Appellant has not reasonably shown that a skilled artisan would expect the same results when formulating a composition with each of the claimed class of active compounds. Thus, assuming arguendo that the Declarations were persuasive, then the claims must be commensurate with the scope.

Appellant argues that the examiner has "intermingled" the concept of showing unexpectedness and lack of enablement.

The examiner has not intermingled these concepts. In the interest of compact prosecution, the examiner has addressed all pertinent issues that have been raised and may be raised by Appellant. It is the examiner's position that the claim language does not exclude Depui's separating layer. However, to address the possible interpretation that the claims may exclude the separating layer, the examiner has addressed the purported evidence that Depui has a non-enabling disclosure. To address Appellant's argument that the claimed process purportedly provides for unexpected stability, the examiner has addressed this also.

Therefore, it is the examiner's position that the prior art renders the instant invention prima facie obvious.

(B) Claims 15-16, 18-25, 30-31, 33-34, 36, 39-46, 49 are rejected under 35 U.S.C. 103(a) as being unpatentable over US Patent 6,132,771 to Depui et al in view of Ohno et al (4,017,647) or Wurster (2,799,241) respectively.

Appellant's arguments pertaining to Depui '771 are substantially similar to those made regarding Depui '184. Therefore, the examiner's response to Depui '184 which addresses the instant claim language, the separating layer, and all the Declarations of record are incorporated herein. The arguments pertaining to Depui '771 are addressed below.

Appellant argues that the Wurster-type fluidized apparatus provides for a uniform coating, which eliminates the need for a separating layer and still provide a stable dosage form. Appellant argues that Ohno does not teach all coating apparatuses are equivalent and the examiner is not free to modify the disclosures. Appellant argues that, "There is not a single mention in this paragraph of a fluidized bed in connection with applying the active ingredient coating or the enteric coating. What is specifically mentioned is rotor granulation or extrusion/spheronization. As already established in the Molina Declaration, the use of rotor granulation produces an inferior and unacceptable product."

Example 4 of Depui '771 discloses utilizing a fluidized apparatus, not a rotor granulation or extrusion/spheronization apparatus, in all three steps use. Thus, Depui clearly teaches a similar apparatus and similar process.

Appellant argues that the Molina affidavit demonstrates that Depui is not enabled. Appellant argues that the Johansson's declaration demonstrates that Depui is not enabling. Appellant argues that the instant example 1 is more stable than Depui's example 5.

First, it is respectfully submitted that Appellant's Declarations and Appellant's arguments in reference to the Declaration are based on the erroneous assertion that the claims exclude a separating layer. However, it is the examiner's position that the instant claim language does not

exclude Depui's separating layer. However, assuming arguendo the claims exclude this layer, the examiner notes the following:

The examiner notes that in the Molina declaration, Appellant attempts to overcome Depui by showing EP 0642797 does not make a stable granule. It is pointed out that if Appellant contends that the prior art is not enabling, and in instant case, Appellant contends Depui is not enabling, then the Declaration must show that Depui is not enabled. Appellant's demonstration that EP '797 does not make a stable granule does not extend to Depui. Depui is a different invention with no relation to EP '797. Further, **EP '797 teaches a different formulation than Depui.** For instance, EP '797 contains excipients used to coat the inert seed that are not utilized in Depui's examples. These excipients may contribute to the lack of stability. For instance, starch is a known disintegrant. The formulations of Depui and EP '797 are not the same. Appellant has not addressed this.

Moreover, it is the Appellant's position that it is not Appellant's burden but the examiner's burden to demonstrate how these excipients cause instability. The examiner respectfully points out that the standard for demonstrating that an issued US patent is not enabling is not only high, but it is Appellant's burden and not the examiner's. The examiner can only determine enablement of the prior art, or conversely, lack thereof, by the evidence given by Appellant. The examiner notes the differences in the formulations which cause the evidence provided by Appellant to be not persuasive since it does not conclusively demonstrate that Depui is not enabled. The examiner has satisfied the criteria of analyzing the evidence to determine if the prior art is enabled for certain embodiments; however Appellant has not satisfied Appellant's burden of demonstrating why these additional excipients disclosed in EP '797 and the difference

in the dosage form do not have a bearing on the issue of enablement. Appellant's refusal and failure to show that *Depui's* dosage form is perplexing since it is Appellant that is attempting to demonstrate that Depui is not enabled for certain embodiments. Thus, it is the examiner's position that Appellant must demonstrate that Depui's dosage form not other prior art dosage forms are not stable.

Regarding the Johansson's Declaration, the Declaration states, "The results obtained in working Example 5 of US 6.132.771 where not a surprise for me, because the prior art, for instance EP0247983 (US 4,786,505) and EP244380 (US 4,853,230) cited in the patent application taught that an inert separating layer should be place between the core material and the outer enteric coating layer to avoid the contact between the anti-ulcer benzimidazole compound (omeprazole, lansoprazole, pantoprazole. etc.) and the acidic component (methacrylic copolymer) of the enteric layer. It is also mentioned that benzimidazole compounds are not stable in acidic medium, and in contact with acidic compounds they suffer degradation and develop a strong color."

The examiner notes the following: The instant invention *as claimed* is directed to the same dosage as disclosed by Depui et al. For instance, Appellant argues that the instant invention does not require Depui's optional separating layer and still is stable. Assuming arguendo that the claims do exclude the separating layer, the examiner notes that the instantly claimed invention requires the core material that comprises the anti-ulcer benzimidazole compound (omeprazole, lansoprazole, pantoprazole. etc.), an alkaline reaction compound, and an enteric coating polymer wherein the instant examples in the specification utilize an acidic polymer. The prior art also discloses this, except the prior art exemplifies an optional separating layer. It is unclear how the

instant formulation is stable versus the prior art's formulation if the only difference is the separating layer, which Appellant argues provides stability to Depui's dosage form. The same dosage form is being claimed; thus the same interaction must take place. The examiner points out that the distinguishable feature must be claimed since Appellant's arguments are on the basis that the prior art is not enabled for a stable formula and the instant invention is. If Appellant removes the stabilizing separating layer of the prior art, what makes the instant invention stabilizing without it? It is further noted that the instant specification does not utilize an alkaline material in combination with the anti-ulcer drug. As argued by Appellant in the background section page 5 of the Appeal Brief, Appellant argues that the alkaline material used to protect the active in the active layer, interacts with the enteric coating to cause degradation. Thus, Appellant stated the prior art requires a separating layer. Therefore, it is noted that Appellant discloses and claims the same dosage form as the prior art and yet argues that the prior art is not enabling. Thus, like Depui, Appellant has not exemplified a dosage form comprising an active layer comprising the alkaline material and anti-ulcer compound without a separating layer.

Appellant attributes the stability to the non-porous layer and argues that Depui does not teach this.

Although Depui does not explicitly state that the layer is substantially non-porous layer, Depui's layer is the same as Appellant's. Thus, Depui's active layer must be substantially non-porous. Appellant argues that Depui's active layer is porous but does not specify what exactly makes it porous. First, it is noted that "substantially" is a broad term and is not defined by the specification. Depui's active layer has the same components as the instant claims and the examples disclosed in Appellant's specification; thus it is the examiner's position that it is non-

porous. The claims are directed to "a *substantially* non-porous active layer made from aqueous or hydroalcoholic solution suspension which comprises an anti-ulcer compound, an alkaline reacting compound, and at least one pharmaceutically acceptable excipient selected from the groups which includes a binder, a surface active agent, a filling material, and a disintegrating swelling excipient". Depui discloses the seeds (inert nucleus) are layered with a water suspension comprising the instant anti-ulcer compound, with the alkaline material, a binder, and surface active agent (surfactant). It is respectfully submitted that when the structure of the prior art is substantially identical to the instant claims, the properties must be the same. The examiner has made a reasonable rationale as to why the active layer is substantially non-porous. However, Appellant has not provided any evidence showing that Depui's layer is not substantially non-porous. Appellant has not even provided any persuasive argument, other than the "prior art does not teach a substantially non-porous layer", why Depui's active layer is not substantially non-porous layer.

Appellant attributes the instant invention's stability to the process of making the composition. Appellant has argued that the process of making the instant invention, i.e. utilizing a Wurster fluidized bed coater, lends to the stability (Response of 10/31/05,12/3/04 and affidavit of 11/22/02).

However, it is noted that Depui also uses a fluid bed apparatus and specifically a Wurster-fluidized apparatus in example 4. Although, it is unclear if the same apparatus is used in all three steps, it is the examiner's position that the process will yield a similar result since the same type of machine is used. It is noted on page 16 of the instant specification. Appellant discloses that a Wurster-type fluid bed apparatus "or a similar equipment" may be used.

Appellant has not compared a process using specifically Wurster-type fluidized apparatus compared to another process using a fluidized bed apparatus. Moreover, Appellant has not provided any evidence that using a Wurster-type fluidized bed apparatus in all three steps compared to using a unspecified fluidized bed apparatus in the first step, followed by using the instant Wurster-type fluidized apparatus provides any unexpected product. For instance, the Rule 132 declaration compares the stability of Depui's formulation US '771 with or without the separating layer to show that Depui '184 is purportedly non-enabling. However, the Declaration does not provide any unexpected results pertaining to the apparatus itself. Further, it is unclear from this Declaration and results if Appellant's stability is due to the Wurster bed coater. The examiner has suggested that Appellant provide evidence wherein two formulas with the same components are made by different apparatuses since this is the purported difference. However, Appellant has not done so.

The Johansson and Molina-Millian Declarations state that the prior art's tablets are discolored compared to the instant invention and this discoloration shows a degradation of the active which is unacceptable.

The examiner respectfully submits that the standard for demonstrating that a reference is not enabling, is high. To demonstrate that a reference is not enabling, the Appellant must demonstrate that a pellet cannot be made. Clearly, a pellet was made, regardless of the color. Regarding the showings of unexpectedness to overcome the 103 rejection, it is pointed out that the discoloration only appeared **after an hour**. The claims do not recite stability parameters, i.e. how long the instant pellets are stable for. Clearly, as evidenced by the declaration, Depui's pellets are stable for at least one hour.

Appellant argues that recited benefits should not be recited in the claims.

Appellant has misinterpreted the examiner. The examiner is merely pointing out that Appellant's assertion that Depui is not enabled since it is not stable is erroneous since the pellet is clearly stable for an hour. Therefore, Depui meets the claimed limitations of dependent claims 39-40 since the claims merely recite the "preparation is stable" without any specific parameters.

Moreover, Appellant's Declaration is solely based on color to show degradation of the active. However, discoloration does not necessarily imply that the active has degraded. The discoloration may be due to the interaction of other components. Appellant has not provided any data showing a chemical analysis of the active and its purported degradation. The mere assertion that the discoloration means that the active has degraded is not enough to show that the prior art is not stable and thus not enabled.

Appellant argues that the Lovgren Patent (US 4786505) indicates that discoloration means degradation. Appellant states that the examiner hypothesizes that the source of degradation is from another source other than degradation. However, Appellant argues that the examiner has not provided any evidence to support such an assertion.

Again, the examiner respectfully points out that it is Appellant's burden and not the examiner's burden to show that the prior art is not enabled. The examiner can only make an analysis based on the evidence provided by Appellant's. The examiner has made such an analysis and has found the evidence insufficient to conclusively demonstrate that Depui is not enabled. A patent is presumed to be valid. Thus, the examiner is not required to prove that the prior art relied upon is enabled. If Appellant is attempting to demonstrate that Depui is <u>not</u> enabled for certain embodiments, then it is Appellant's burden to do so. Appellant has not shown

conclusively that discoloration necessarily means that the active has degraded. The examiner notes that Lovgren in fact teaches that although some pellets have a slight discoloration, the pellets were stable. Note the examples.

Furthermore, it is noted that the claims are not commensurate in scope. Appellant relies on example 1 of the instant specification to demonstrate that the prior art is not enabled and that the instant invention is unexpectedly stable. Example 1 of the instant specification discloses a charged nucleus and the enteric coating with specific materials whereas the instant claims are broadly directed at least one excipient. As discussed above, Appellant claims the same dosage form and states the difference between the prior art and the instant invention is the use of a separating layer. Further, Appellant argues this separating layer in the prior art functions to provide stability. Thus, the question is, how does Appellant obtain a stable pellet by removing the stabilizing stable layer? It is noted that in inventive example 1, the charged nucleus and the enteric coat comprises the components of the prior art's separating layer. For instance, the Depui's separating layer (example 4) comprises HPMC, PEG 6000, and talc whereas although the instant invention excludes the separating layer, the charged nucleus composition comprises HPMC and the enteric coating composition comprises talc and PEG 6000. Thus, if Appellant's stability is due to adding the very components that comprises the prior art's separating layer, to the charged nucleus and enteric coating respectively (thus eliminating the need for the prior art's separating layer), then Appellant must claim this. Further, specific excipients are utilized in specific concentrations and it is unclear if the excipient and its concentrations contribute to the stability of the instant invention. Lastly, the examiner notes that Appellant's independent claims are drawn to several different classes of compounds and Appellant emphasizes the stability of the

compounds. Appellant's Rule 132 is directed to a single species lanzoprazole in a specific formula. However, a single species cannot extend patentability to the entire genus and Appellant has not reasonably shown that a skilled artisan would expect the same results when formulating a composition with each of the claimed class of active compounds. Thus, assuming arguendo that the Declarations were persuasive, then the claims must be commensurate with the scope.

Appellant argues that the examiner has "intermingled" the concept of showing unexpectedness and lack of enablement.

The examiner has not intermingled these concepts. In the interest of compact prosecution, the examiner has addressed all pertinent issues that have been raised and may be raised by Appellant. It is the examiner's position that the claim language does not exclude Depui's separating layer. However, to address the possible interpretation that the claims may exclude the separating layer, the examiner has addressed the purported evidence that Depui has a non-enabling disclosure. To address Appellant's argument that the claimed process purportedly provides for unexpected stability, the examiner has addressed this also.

Regarding Ohno, the examiner has cited the exact portion which has argued the examiner has modified. Ohno teaches all coaters act under the same principle. On column 3, lines 24-40, Ohno teaches, "Any conventional coating machines, for example, pan coaters, rotary drum-type coaters, such as, Accela-Cota manufactured by Manesty Machines, England, Wurster-type fluidizing coaters developed by Wisconsin Alumuni Research Foundation, U.S.A., and fluidizing coaters such as that manufactured by Glatt, West Germany, may be employed in the method of the invention. There is no difference in principle between the conditions with which the solid dosage forms are coated in accordance with the invention and those with which the

abovementioned conventional coaters are operated using a coating solution with an organic solvent." Thus, it can be seen that the examiner has modified Ohno's disclosure and this is sufficient to establish a prima facie case of obviousness. Moreover, Depui teaches a fluidized bed apparatus in all three steps. The only teaching lacking is the type of fluidized apparatus. Wurster teaches that the Wurster-equipped fluidized apparatus provides a uniform coating. Thus, it is the examiner's position absent unexpected results (the examiner has discussed the Declarations and the purported unexpectedness above), that a skilled artisan would have been motivated to specifically use the Wurster-equipped fluidized apparatus to provide a uniform coating. Further, Appellant has not provided any evidence that the Wurster-type bed coater provide the unexpected results. For instance, the Rule 132 Declaration compares the stability of Depui's formulation with or without the separating layer to show that Depui is supposedly non-enabling. However, the Declaration does not provide any unexpected results pertaining to the apparatus itself. It is unclear from this Declaration and results if Appellant's stability is due to the Wurster bed coater.

Appellant argues that Wurster only teaches tablets, chewing gums, candies, and nuts. Appellant argues Wurster does not mention pellet cores or that this type of apparatus can be operated so as to obtain a substantially non-porous soluble active layer which can eliminate the need for a separating layer.

Again, it is the examiner's position that the instant claim language does not exclude Depui's separating layer. The examiner's response to the separating layer has been discussed in the Response to Arguments Section of Depui '184 which is incorporated herein. Further, it is the examiner's position that Depui '771 is not deficient in the disclosure of a *substantially* non-

porous layer as discussed above. Depui's example 5 discloses lanzoprazole, sugar sphere seeds, hydroxypropylmethyl cellulose, sodium laurylsulfate, and water. Instant example 2 on page 18 of the instant specification discloses lanzoprazole, sodium lauryl sulphate, hydroxypropylmethyl cellulose, crystallized disodium phosphate, lactose, hydroxypropyl cellulose, and water. The instant example and Depui's example 5 are similar and thus the layer must necessarily be non-porous. Depui need not explicitly state all the implicit properties of the active layer. Thus, the only deficiency in Depui '771 is the specific use of a Wurster fluidized apparatus. Therefore, Wurster is not relied upon to teach a pellet core or a substantially non-porous soluble active layer.

Therefore, it is the examiner's position that the prior art renders the instant invention prima facie obvious.

(C) Claims 15-16, 18-25, 30-31, 33-34, 36, 39-46, 49 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO 96/01624 in view of Ohno et al (4,017,647) or Wurster (2,799,241).

Appellant's arguments pertaining to WO '624 are substantially similar to those made regarding Depui '184 and Depui '771. Therefore, the examiner's response to Depui '184 which addresses the instant claim language, the separating layer, and all the Declarations of record are incorporated herein. Further, the examiner's response to Ohno and Wurster are incorporated herein. The arguments pertaining to WO '624 are addressed below.

The Johansson and Molina-Millian Declarations state that the prior art's tablets are discolored compared to the instant invention and this discoloration shows a degradation of the active which is unacceptable.

The examiner respectfully submits that the standard for demonstrating that a reference is not enabling, is high. To demonstrate that a reference is not enabling, the Appellant must demonstrate that a pellet cannot be made. Clearly, a pellet was made, regardless of the color. Regarding the showings of unexpectedness to overcome the 103 rejection, it is pointed out that the discoloration only appeared **after an hour**. The claims do not recite stability parameters, i.e. how long the instant pellets are stable for. Clearly, as evidenced by the declaration, the pellets are stable for at least one hour.

Appellant argues that recited benefits should not be recited in the claims.

Appellant has misinterpreted the examiner. The examiner is merely pointing out that Appellant's assertion that Depui is not enabled since it is not stable is erroneous since the pellet is clearly stable for an hour. Therefore, Depui meets the claimed limitations of dependent claims 39-40 since the claims merely recite the "preparation is stable" without any specific parameters.

Moreover, Appellant's Declaration is solely based on color to show degradation of the active. However, discoloration does not necessarily imply that the active has degraded. The discoloration may be due to the interaction of other components. Appellant has not provided any data showing a chemical analysis of the active and its purported degradation. The mere assertion that the discoloration means that the active has degraded is not enough to show that the prior art is not stable and thus not enabled.

Appellant argues that the Lovgren Patent (US 4786505) indicates that discoloration means degradation. Appellant states that the examiner hypothesizes that the source of degradation is from another source other than degradation. However, Appellant argues that the examiner has not provided any evidence to support such an assertion.

Again, the examiner respectfully points out that it is Appellant's burden and not the examiner's burden to show that the prior art is not enabled. The examiner can only make an analysis based on the evidence provided by Appellant's. Appellant has not shown conclusively that discoloration necessarily means that the active has degraded. The examiner notes that Lovgren in fact teaches that although some pellets have a slight discoloration, the pellets were stable. Note the examples.

Appellant argues that WO '624 does not teach a substantially non-porous homogeneous layer.

Although WO '624 does not explicitly state that the layer is substantially non-porous layer, WO '624 discloses the same layer as Appellant. Thus, the prior art's active layer must be substantially non-porous. Appellant argues that WO's active layer is porous but does not specify what exactly makes it porous. First, it is noted that "substantially" is a broad term and is not defined by the specification. WO's active layer has the same components as the instant claims and the examples disclosed in Appellant's specification; thus it is the examiner's position that it is non-porous. The claims are directed to "a *substantially* non-porous active layer made from aqueous or hydroalcoholic solution suspension which comprises an anti-ulcer compound, an alkaline reacting compound, and at least one pharmaceutically acceptable excipient selected from the groups which includes a binder, a surface active agent, a filling material, and a disintegrating swelling excipient". WO '624 discloses the seeds (inert nucleus) are layered with a water suspension comprising the instant anti-ulcer compound, with the alkaline material, a binder, and surface active agent (surfactant). It is respectfully submitted that when the structure of the prior art is substantially identical to the that of the claims, the properties must be the same. The

examiner has made a reasonable rationale as to why the active layer is substantially non-porous. However, Appellant has not provided any evidence showing that WO's layer is not substantially non-porous.

Therefore, it is the examiner's position that the prior art renders the instant invention prima facie obvious.

(D) Claims 47-48 and 50 are rejected under 35 U.S.C. 103(a) as being unpatentable over US Patent to Depui et al (6,365,184) in view of Wurster (2,799,241) in view of Palomo (5,232,706) in further view of Kim et al (5,219,870).

Appellant does not argue the merits of the instant rejection and rather argues the references individually. Appellant merely argues that Palomo discloses an intermediate coating and merely identifies certain additional basic compounds. Appellant argues that Kim does not solve the problem of rapid degradation of the proton pump inhibitors. Appellant argues that a skilled artisan would not look to Kim since the present invention's problem is not encountered by Kim.

The examiner acknowledges Palomo discloses other basic compounds that may be used with the instant anti-ulcer compounds; this is the premise of the rejection. The examiner relies on Palomo and Kim to teach the claimed amino acids since Depui only suggests the use of amino acids in general. Kim is not relied upon to teach the problems of rapid degradation of anti-ulcer compounds since this is not the premise of the rejection However, it is noted that Kim teaches amino acids provide stability and prevent the anti-ulcer compounds from degrading. Therefore, Appellant's unexpected property of providing a stable pellet is actually taught by Kim.

(E) Claims 47-48 and 50 are rejected under 35 U.S.C. 103(a) as being unpatentable over US Patent to Depui et al (6,132,771) or WO 96/01624 respectively, in view of Ohno et al (4,017,647) or Wurster (2,799,241) respectively, in view of Palomo (5,232,706) in further view of Kim et al (5,219,870).

Appellant does not argue the merits of the instant rejection and rather argues the references individually. Appellant merely argues that Palomo discloses an intermediate coating and merely identifies certain additional basic compounds. Appellant argues that Kim does not solve the problem of rapid degradation of the proton pump inhibitors. Appellant argues that a skilled artisan would not look to Kim since the present invention's problem is not encountered by Kim.

The examiner acknowledges Palomo discloses other basic compounds that may be used with the instant anti-ulcer compounds; this is the premise of the rejection. The examiner relies on Palomo and Kim to teach the claimed amino acids since Depui only suggests the use of amino acids in general. Kim is not relied upon to teach the problems of rapid degradation of anti-ulcer compounds since this is not the premise of the rejection However, it is noted that Kim teaches amino acids provide stability and prevent the anti-ulcer compounds from degrading. Therefore, Appellant's unexpected property of providing a stable pellet is actually taught by Kim.

(11) Related Proceeding(s) Appendix

No decision rendered by a court or the Board is identified by the examiner in the Related Appeals and Interferences section of this examiner's answer.

For the above reasons, it is believed that the rejections should be sustained.

Respectfully submitted,

Sharmila Gollamudi Landau

/Sharmila Gollamudi Landau/

Primary Examiner, Art Unit 1611

Conferees:

Michael Woodward

/MP WOODWARD/

Supervisory Patent Examiner, Art Unit 1615

/Robert A. Wax/
Robert A. Wax
TQAS Appeals Specialist
Technology Center 1600